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09/734,583	12/13/2000	Vered Hornik	2254-030	3691

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EXAMINER
AUDET, MAURY A

ART UNIT	PAPER NUMBER
1654	

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7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/734,583	Applicant(s) HORNIK ET AL.	
	Examiner Maury Audet	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *19-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2(part)* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept.

In accordance with 37 CFR 1.142, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 1-18, drawn to a somatostatin peptide compounds, classified in class 530, subclass 300+.

II. Claim 19-21, drawn to a method of treating 10 broad disease categories using a somatostatin peptide compound, classified in class 514, subclass 2.

III. Claim 22-24, drawn to a method of diagnosing cancer treating 10 broad disease categories using a somatostatin peptide compound, classified in class 424, subclass 9.34.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II-III are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the process for using the product as claimed can be practiced with another materially different product, as evident by the myriad of peptide formulas and

compounds (i.e. claim 15) capable of use therein. Therefore, the inventions are patentably distinct.

The methods of Groups II-III are directed to different inventions, which are not connected in design, operation, and/or effect. These methods are independent since they are not disclosed as capable of use together, they have different modes of operation, they have different functions, and/or they have different effects. One would not have to practice the various methods at the same time to practice just one method alone.

The several inventions above are independent and distinct, each from the other. They have acquired a separate status in the art as a separate subject for inventive effect and require independent searches. The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference, which would anticipate the invention of one group, would not necessarily anticipate or even make obvious another group. Finally, the consideration for patentability is different in each case. Thus, it would be an undue burden to examine all of the above inventions in one application. Restriction for examination purposes is therefore proper.

Because these inventions are distinct for the reasons given above and the search required for each group is not necessarily required for the other groups, restriction for examination purposes as indicated is proper.

Species Election

This application contains claims directed to the following patentably distinct species of the claimed invention: backbone cyclized somatostatin analogs of the present invention drawn to six different formulas as well as 10 distinctly claimed variants in claim 15.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species (one complete analog) for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 1 is generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CRF 1.143).

Applicant is reminded that upon cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

During a telephone conversation with Allan Fanucci on 6/16/03, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-18; and the analog species number 8 of 10 in claim 15 (Phe(C3)-Cys*-Phe-(D)Trp-Lys-Thr-Phe-Gly(S2)-X (where X is OH). Affirmation of this election must be made by applicant in replying to this Office action. Claims 19-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Information Disclosure Statement

The information disclosure statement filed on 8/20/01 does not fully comply with the requirements of 37 CFR 1.98 because: copies of the references could not be found in the parent applications or in the present application. The 12 U.S. patent references have been considered, based on an independent search and consideration by the Examiner of these references in the USPTO database; however, the "Foreign Patent Documents" and "Other References" have not been considered and copies of each must be resubmitted. Since the submission appears to be *bona fide*, applicant is given **ONE (1) MONTH** from the date of this notice to supply the above mentioned omissions or corrections in the information disclosure statement. NO EXTENSION OF THIS TIME LIMIT MAY BE GRANTED UNDER EITHER 37 CFR 1.136(a) OR (b).

Failure to timely comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the noncomplying information **not** being considered. See 37 CFR 1.97(i).

Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 recites the limitation "CO-(CH2)n" in the bridging group, without claiming "Y" in between the above, in Formula No. 7. There is insufficient antecedent basis for this limitation in the claim. Claim 1 distinctly claims that the compound must have "a bridging group comprising an amide, thioether, thioester, or disulfide". The other claims define that "Y" (however see below 112 2nd on Y versus Y2) is the label used to define the bridging groups amide, thioether, thioester, or disulfide. In order to properly depend from claim 1, it is strongly suggested that "Y" (or Y2) be inserted between between the CO and (CH2)n of Formula No. 7, and also be defined thereafter.

In claims 5, and 9-13, it is unclear what "Y2" is referencing in the respective formulas, since only "Y" is identified in the respective formulas. For instance, in claim 7, "Y" is identified

and defined as "an amide, thioether, thioester, or disulfide". Thus, it is unclear what "Y2" refers to?

In the amended claims 5, and 9-14, it is stated after the claim number that the listed claims are "(currently amended)"; however, there are no underlined portions indicating what has been amended. Furthermore, claim 13, should stated "(previously amended)", as it was amended previously, like claim 15.

Appropriate correction is required.

35 U.S.C. § 103 Obviousness

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arad et al. (including Applicant's Afargan Gellerman, Hornik; Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), I & EC-012. American Chemical Society: Washington, D.C.)) in view of Kaljuste et al. (Int J Pept Protein Res. 1994 May;43(5):505-11).

Arad et al. teach "[b]ackbone-cyclization of peptides [specifically the Somatostatin family] is accomplished *via a bridge between two backbone amide nitrogens* [citing C. Gilon et al., Biopolymers, 1991, 31, 745]. *Backbone-cyclization can be carried out between any two residues in the sequence* without altering the side chains of the amino acid residues involved in the cyclization" and that a "*significant increase in biostability and in selectivity* is seen upon

cyclization" (abstract; emphasis added). Arad et al. does not expressly teach an amide, thioether, thioester, or disulfide attached between the backbone amine nitrogens or expressly that "the sequence includes a non-cyclized chain of 4, 5, or 6 amino acids" [Applicant's claim 1].

Kaljuste et al. teaches a new solid-phase method for the synthesis of backbone-to-backbone cyclyzed peptides, for peptides generally. Specifically, Kaljuste et al. teach Applicant's "N building unit-bridging group [disulfide]-N building unit" (i.e. "N-CH2-CH2-CH2S – SCH2-CH2-CH2-N" and a non-cyclized chain of 4, 5, or 6 amino acids between the cyclized residues (see specification formulas to compounds). Kaljuste et al. does not expressly teach that the peptide cyclized is somatostatin.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to cyclize somatostatin between two backbone amide nitrogen's of Arad et al. using the disulfide bond attachment between the backbone amine nitrogens and having the "non-cyclized chain of 4, 5, or 6 amino acids" of Kaljuste et al., because Kaljuste et al. teach the beneficial cyclization of a small peptide (10-mer) between backbone N's of the sequence with a disulfide bond there between; wherein the bridge spans across "a non-cyclized chain of 4, 5, or 6 amino acids".

Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Arad et al. (including Applicant's Afargan Gellerman, Hornik; Book of Abstracts, 211th ACS National Meeting, New Orleans, LA, March 24-28 (1996), I & EC-012. American Chemical Society: Washington, D.C.)) in view of Kaljuste et al. (Int J Pept Protein Res. 1994 May;43(5):505-11), and further in view of Bauer et al. (US 4,395,403).

Arad et al. and Kaljuste et al. are both discussed above. Neither reference expressly teaches Applicant's elected peptide sequence (species number 8 of 10 in claim 15 (Phe(C3)-Cyx*-Phe-(D)Trp-Lys-Thr-Phe-Gly(S2)-X (where X is OH)).

Bauer et al. teach a backbone cyclized somatostatin analog of the same sequence as Applicant's elected analog and cyclized through the same residues (Cys 2 and 7)(column 1, 3rd ¶). Bauer et al. teach the cyclization through the S of the Cys amino acids (id.). Although Bauer et al. teaches that "compounds may be produced by methods known in the art of peptide chemistry or by obvious chemical equivalents" (column 4, lines 57-59); Bauer et al. does not expressly teach that the cyclization through an "N" of either cyclized Cys residue.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to cyclize a specific-length somatostatin analog between two backbone amide nitrogen's of Arad et al. (specifically cyclization of the elected 8-mer sequence between the backbone Cys N's and disulfides), in view of Kaljuste et al. and Bauer et al., because Kaljuste et al., as discussed above, teach the beneficial cyclization of a small peptide (10-mer) between backbone N's of the sequence with a disulfide bond there between; and further because Bauer et al. teach the advantageous use of the desired sequence structure cyclized through the backbone Cys residues (at 2 and 7 positions) and that obvious chemical equivalents (i.e. N and disulfide cyclization) are within the spirit of the invention.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at

the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 5,770,687 ('687 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. (NOTE: The '554 Patent and '613 Patent, discussed below and which provide priority for the present continuation application, are also both subject to a Terminal Disclaimer in view of the '687 Patent).

The claims of the '687 Patent are drawn to cyclic somatostatin analogs. The claims of the '687 Patent encompass the claimed invention since the generic claim 1 of the '687 Patent discloses similar variables for R5-R12 as the presently claimed invention. For example, the generic peptide of claim 1 of the '687 Patent encompasses the peptide, for instance of claim 9

when, in the US Patent variable R5 is absent, R6 and R11 are Phe, R7 is Phe or Tyr, R10 is Thr, and R12 is Val.

Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,051,554 ('554 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims of the '554 Patent are drawn to cyclic somatostatin analogs. The claims of the '554 Patent encompass the claimed invention since the generic claim 1 of the '554 Patent discloses a similar generic claim (". . . a peptide sequence of four to twelve amino acids that incorporates at least two building units, each of which contains one nitrogen atom of the peptide backbone connected to a bridging group comprising an amide, thioether, thioester or disulfide, wherein the at least two building units are connected to the bridging group to form a cyclic structure"). Additionally, the '554 Patent discloses similar variables for R5-R12 as the presently claimed invention (see for example claim 7 in both).

Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2-41 of U.S. Patent No. 6,355,613 B1 ('613 Patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims of the '613 Patent are drawn to cyclic somatostatin analogs. The claims of the '613 Patent encompass the claimed invention since the generic claim 1 of the '613 Patent

discloses a similar generic claim (". . . a peptide sequence of four to twelve amino acids that incorporates at least one building unit, said building unit containing one nitrogen atom of the peptide backbone connected to a bridging group comprising an amide, thioether, thioester or disulfide, wherein the at least one building unit is connected to the bridging group to a second building unit, a side chain of an amino acid residue of the peptide sequence, or an N-terminal amino acid residue to form a cyclic structure"). Additionally, the '613 Patent discloses similar variables for R5-R12 as the presently claimed invention (see claims).

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 703-305-5039. The examiner can normally be reached from 7:00 AM – 5:30 PM, off Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached at 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-1234 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

MA
September 15, 2003

CHRISTOPHER R. TATE
PRIMARY EXAMINER